CLAIMS

We claim:

1. A biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

a drug;

a first component comprising at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula $Compound_1$ - $(SH)_m$, wherein $m \geq 2$; and

a second component comprising at least one sulfhydryl reactive group-containing compound in either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula $Compound_2$ -Y_n, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$;

wherein at least one of the first or second components is a polyalkylene oxide and wherein the sulfhydryl groups and the sulfhydryl reactive groups react with one another to form covalent bonds therebetween when said components are mixed together to form a gel in less than one minute.

2. The composition of claim 1, wherein m and n are each 4.

3. The composition of claim 1, wherein m and n are each 12.

4. The composition of claim 1, wherein the first component is a polyalkylene oxide.

5. The composition of claim 1, wherein the second component is a polyalkylene oxide.

6. The composition of claim 1, wherein the first and second components are polyalkylene oxides.

7. The composition of claim 6, wherein the polyalkylene oxides are polyethylene glycol.

8. The composition of claim 1, wherein only one of the first or second components is a polyalkylene oxide.

9. The composition of claim 8, wherein one of the components is a polyalkylene oxide and the other component is a functionally activated succinimidyl or maleimidyl compound which is not a polymer.

10. The composition of claim 1, wherein the covalent bonds are thioester linkages.

11. The composition of claim 1, wherein the covalent bonds are thioether linkages.

12. The composition of claim 1, wherein the covalent bonds are sulfhydryl linkages.

13. The composition of claim 1, wherein the drug is hydrophobic.

14. The composition of claim 1, wherein the drug is an angiogenesis inhibitor.

15. The composition of claim 1, wherein the drug is a 5-Lipoxygenase inhibitor or antagonist.

16. The composition of claim 1, wherein the drug is a chemokine receptor antagonist.

17. The composition of claim 1, wherein the drug is a cell cycle inhibitor or an analogue or derivative thereof.

18. The composition of claim 17, wherein the cell cycle inhibitor is a microtubule stabilizing agent.

19. The composition of claim 18, wherein the microtubule stabilizing agent is paclitaxel, docetaxel, or Peloruside A.

20. The composition of claim 17, wherein the cell cycle inhibitor is a taxane.

21. The composition of claim 18, wherein the taxane is paclitaxel or an analogue or derivative thereof.

22. The composition of claim 17, wherein the cell cycle inhibitor is an antimetabolite, an alkylating agent, or a vinca alkaloid.

23. The composition of claim 22, wherein the vinca alkaloid is vinblastine, vincristine, vincristine sulfate, vindesine, vinorelbine, or an analogue or derivative thereof.

24. The composition of claim 17, wherein the cell cycle inhibitor is camptothecin or an analogue or derivative thereof.

25. The composition of claim 17, wherein the cell cycle inhibitor is selected from the group consisting of mitoxantrone, etoposide, 5-fluorouracil,

doxorubicin, methotrexate, Mitomycin-C, CDK-2 inhibitors, and analogues and derivatives thereof.

26. The composition of claim 1, wherein the drug is a cyclin dependent protein kinase inhibitor or an analogue or derivative thereof.

27. The composition of claim 1, wherein the drug is an EGF (epidermal growth factor) kinase inhibitor or an analogue or derivative thereof.

28. The composition of claim 1, wherein the drug is an elastase inhibitor or an analogue or derivative thereof.

29. The composition of claim 1, wherein the drug is a factor Xa inhibitor or an analogue or derivative thereof.

30. The composition of claim 1, wherein the drug is a farnesyltransferase inhibitor or an analogue or derivative thereof.

31. The composition of claim 1, wherein the drug is a fibrinogen antagonist or an analogue or derivative thereof.

32. The composition of claim 1, wherein the drug is a guanylate cyclase stimulant or an analogue or derivative thereof.

33. The composition of claim 1, wherein the drug is a heat shock protein 90 antagonist or an analogue or derivative thereof.

34. The composition of claim 1, wherein the drug is an HMGCoA reductase inhibitor or an analogue or derivative thereof.

35. The composition of claim 1, wherein the drug is a hydroorotate dehydrogenase inhibitor or an analogue or derivative thereof.

36. The composition of claim 1, wherein the drug is an IKK2 inhibitor or an analogue or derivative thereof.

37. The composition of claim 1, wherein the drug is an IL-1, ICE, or IRAK antagonist or an analogue or derivative thereof.

38. The composition of claim 1, wherein the drug is an IL-4 agonist or an analogue or derivative thereof.

39. The composition of claim 1, wherein the drug is an immunomodulatory is rapamycin, tacrolimus, everolimus, biolimus, or an analogue or derivative thereof.

40. The composition of claim 1, wherein the drug is an inosine monophosphate dehydrogenase inhibitor or an analogue or derivative thereof.

41. The composition of claim 1, wherein the drug is a leukotreine inhibitor or an analogue or derivative thereof.

42. The composition of claim 1, wherein the drug is a MCP-1 antagonist or an analogue or derivative thereof.

43. The composition of claim 1, wherein the drug is a MMP inhibitor or an analogue or derivative thereof.

44. The composition of claim 1, wherein the drug is a NF kappa B inhibitor or an analogue or derivative thereof.

45. The composition of claim 1, wherein the drug is a NO antagonist or an analogue or derivative thereof.

46. The composition of claim 1, wherein the drug is a P38 MAP kinase inhibitor or an analogue or derivative thereof.

47. The composition of claim 1, wherein the drug is a phosphodiesterase inhibitor or an analogue or derivative thereof.

48. The composition of claim 1, wherein the drug is a TGF beta Inhibitor or an analogue or derivative thereof.

49. The composition of claim 1, wherein the drug is a thromboxane A2 antagonist or an analogue or derivative thereof.

50. The composition of claim 1, wherein the drug is a TNFa Antagonist, a TACE, or an analogue or derivative thereof.

51. The composition of claim 1, wherein the drug is a tyrosine kinase inhibitor or an analogue or derivative thereof.

52. The composition of claim 1, wherein the drug is a vitronectin inhibitor or an analogue or derivative thereof.

53. The composition of claim 1, wherein the drug is a fibroblast growth factor inhibitor or an analogue or derivative thereof.

54. The composition of claim 1, wherein the drug is a protein kinase inhibitor or an analogue or derivative thereof.

55. The composition of claim 1, wherein the drug is a PDGF receptor kinase inhibitor or an analogue or derivative thereof.

56. The composition of claim 1, wherein the drug is an endothelial growth factor receptor kinase inhibitor or an analogue or derivative thereof.

57. The composition of claim 1, wherein the drug is a retinoic acid receptor antagonist or an analogue or derivative thereof.

58. The composition of claim 1, wherein the drug is a platelet derived growth factor receptor kinase inhibitor or an analogue or derivative thereof.

59. The composition of claim 1, wherein the drug is a fibrinogin antagonist or an analogue or derivative thereof.

60. The composition of claim 1, wherein the drug is an antimycotic agent or an analogue or derivative thereof.

61. The composition of claim 1, wherein the drug is a bisphosphonate or an analogue or derivative thereof.

62. The composition of claim 1, wherein the drug is a phospholipase A1 inhibitor or an analogue or derivative thereof.

63. The composition of claim 1, wherein the drug is a histamine H1/H2/H3 receptor antagonist or an analogue or derivative thereof.

64. The composition of claim 1, wherein the drug is a macrolide antibiotic or an analogue or derivative thereof.

65. The composition of claim 1, wherein the drug is an GPIIb IIIa receptor antagonist or an analogue or derivative thereof.

66. The composition of claim 1, wherein the drug is an endothelin receptor antagonist or an analogue or derivative thereof.

67. The composition of claim 1, wherein the drug is a peroxisome proliferators-activated receptor agonist or an analogue or derivative thereof.

68. The composition of claim 1, wherein the drug is an estrogen receptor agent or an analogue or derivative thereof.

69. The composition of claim 1, wherein the drug is somatostatin or an analogue or derivative thereof.

70. The composition of claim 1, wherein the drug is a JNK Kinase inhibitor or an analogue or derivative thereof.

71. The composition of claim 1, wherein the drug is a melanocortin or an analogue or derivative thereof.

72. The composition of claim 1, wherein the drug is a raf kinase inhibitor or analogue or derivative thereof.

73. The composition of claim 1, wherein the drug is a lysylhydroxylase inhibitor or an analogue or derivative thereof.

74. The composition of claim 1, wherein the drug is an IKK 1/2 inhibitor or an analogue or derivative thereof.

75. The composition of claim 1, further comprising an anti-inflammatory agent, an antithrombotic agent, an antibiotic, or a combination thereof.

76. The composition of claim 1, wherein the drug further comprises a polymer.

77. The polymer of claim 76, wherein the polymer is a polymer or copolymer comprising one or more of the residue units of the monomers, lactic acid, glycolic acid, D-lactide, L-lactide, D,L-lactide, glycolide, ε-caprolactone, trimethylene carbonate, 1,4-dioxane-2-one or 1,5-dioxepan-2one,

78. The polymer of claim 77, wherein the polymer is a block copolymers of the for A-B, A-B-A or B-A-B where A is a poly(alkylene oxide) and B is a degradable polyester.

79. The poly(alkylene oxide) in claim 78, wherein the poly(alkylene oxide) is poly(ethylene glycol), poly(propylene glycol), copolymers of ethylene oxide and propylene oxide or mono alkyl ethers thereof

80. The composition of claim 76, wherein the polymer is in the form of a microsphere.

81. The composition of claim 76, wherein the polymer is in the form of a nanosphere.

82. The composition of claim 76, wherein the polymer is in the form of a micelle.

83. The composition of claim 1, wherein the drug further comprises a non-polymeric carrier.

84. The composition of claim 1, wherein the drug is a hydrophobic drug in admixture with a secondary carrier to provide drug/carrier, the drug/carrier being in admixture with the first component to provide drug/carrier/first component, the drug/carrier/first component being suspended in an aqueous buffer solution.

85. The composition of claim 1, wherein the drug is hydrophilic.

86. The composition of claim 1, wherein the drug is a hydrophilic drug in admixture with a secondary carrier to provide drug/carrier, the drug/carrier being in admixture with the first component to provide drug/carrier/first component, the drug/carrier/first component being suspended in an aqueous buffer solution.

87. The composition of claim 1, wherein the first component is suspended in a buffer solution comprising a mixture of phosphate buffer and carbonate buffer.

88. The composition of claim 2, wherein the second component comprises a mixture of succinimidyl polyalkylene oxide and maleimidyl polyalkylene oxide.

89. A method for treating tissues, comprising the steps of:

administering to a tissue site a first component comprising at least one sulfhydryl group-containing compound in liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula $Compound_1$ -$(SH)_m$, wherein $m \geq 2$; and

simultaneously or subsequently administering to the tissue site a second component comprising at least one sulfhydryl reactive group-containing compound either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula $Compound_2$ -Y_n, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$, and wherein at least one of the first or second components is a polyalkylene oxide; and

simultaneously or subsequently administering to the tissue site a drug; and

allowing the sulfhydryl groups and the sulfhydryl reactive groups to react with one another to form covalent bonds therebetween to form a gel in less than one minute.

90. A biocompatible gel-forming drug-delivering composition for *in vivo* administration with a gel time of less than one minute, comprising:

polyalkylene oxide-$(SH)_4$ and drug in a liquid medium having a pH of between 8 and 10.5; and

polyalkylene oxide-Y_4, wherein Y is succinimidyl, in a liquid medium having an acidic pH.

91. A biocompatible gel-forming drug-delivering composition for *in vivo* administration with a gel time of less than one minute, comprising:

polyalkylene oxide-$(SH)_{12}$ and drug in a liquid medium having an alkaline pH; and

polyalkylene oxide-Y_{12} in a liquid medium having an acidic pH, wherein Y is a succinimidyl or maleimidyl group.

92. A biocompatible gel-forming composition for *in vivo* administration, comprising:

a sulfhydryl group-containing polyalkylene oxide in a liquid medium having an acidic pH, wherein said sulfhydryl group-containing polyalkylene oxide is given by the formula Core-$(SH)_m$, wherein $m \geq 2$;

a buffer solution with an alkaline pH; and

drug in admixure with the polyalkylene oxide and/or the buffer solution;

wherein the sulfhydryl groups react with one another to form covalent bonds therebetween when said components are mixed together to form a gel in less than one minute.

93. A biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula $Compound_1$ -$(SH)_m$, wherein $m \geq 2$;

at least one sulfhydryl reactive group-containing compound either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula $Compound_2$ -Y_n, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$;

at least one drug in admixture with either or both of the at least one sulfhydryl group-containing compound and the at least one sulfhydryl reactive group-containing compound; and

collagen;

wherein at least one of either the sulfhydryl group-containing compound or the sulfhydryl reactive group-containing compound is a polyalkylene oxide, and wherein the sulfhydryl groups and the sulfhydryl reactive groups are capable of reacting with one another to form covalent bonds therebetween.

94. The composition of claim 93, wherein m and n are each 4.

95. The composition of claim 93, wherein m and n are each 12.

96. The composition of claim 93 wherein the sulfhydryl group-containing compound is a polyalkylene oxide.

97. The composition of claim 93, wherein the sulfhydryl reactive group-containing compound is a polyalkylene oxide.

98. The composition of claim 93, wherein both the sulfhydryl group-containing compound and the sulfhydryl reactive group-containing compound are polyalkylene oxides.

99. The composition of claim 98, wherein both the sulfhydryl group-containing compound and the sulfhydryl reactive group-containing compound are polyalkylene oxides.

100. The composition of claim 93, wherein only one of the first or second components is a polyalkylene oxide.

101. The composition of claim 100, wherein one of the components is a polyalkylene oxide and the other component is a functionally activated succinimidyl or maleimidyl compound which is not a polymer.

102. The composition of claim 93, wherein the covalent bonds are thioester linkages.

103. The composition of claim 93, wherein the covalent bonds are thioether linkages.

104. The composition of claim 93, wherein the covalent bonds are sulfhydryl linkages.

105. The composition of claim 93, wherein the drug is a hydrophobic drug.

106. The composition of claim 93, wherein the drug is a hydrophobic drug in admixture with a secondary carrier to provide drug/carrier, the drug/carrier being in admixture with either or both of the at least one sulfhydryl group-containing compound and the at least one sulfhydryl reactive group-containing compound.

107. The composition of claim 93, wherein the sulfhydryl group-containing compound is suspended in a buffer solution comprising a mixture of phosphate buffer and carbonate buffer.

108. The composition of claim 93, wherein the sulfhydryl reactive group-containing compound comprises a mixture of succinimidyl polyalkylene oxide and maleimidyl polyalkylene oxide.

109. The composition of claim 93, wherein the collagen is methylated collagen.

110. A biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

(a) a first component in a liquid medium having an acidic pH comprising:

(i) at least one sulfhydryl group-containing compound given by the formula $Compound_1$ $-(SH)_m$, wherein $m \geq 2$;

(ii) at least one sulfhydryl reactive group-containing compound given by the formula $Compound_2$ $-Y_n$, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$; and

(iii) collagen; and

(b) a second component comprising a buffer having a pH of between 8 and 10.5;

wherein a drug is present in admixture with either or both of the first component or the second component; and

wherein at least one of either the sulfhydryl group containing compound or the sulfhydryl reactive group containing compound is a polyalkylene oxide.

111. The composition of claim 110 wherein the collagen is methylated collagen.

112. The composition of claim 110 wherein the second component is a buffer solution comprising a mixture of phosphate buffer and carbonate buffer.

113. A method for forming a drug delivery composition, comprising

a) selecting a first component, a second component and a drug, wherein

the first component comprises at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula $Compound_1$ $-(SH)_m$, wherein $m \geq 2$; and

the second component comprises at least one sulfhydryl reactive group-containing compound in either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula $Compound_2$ $-Y_n$, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$;

at least one of the first or second components is a polyalkylene oxide;

the sulfhydryl groups and the sulfhydryl reactive groups react with one another to form covalent bonds therebetween when said components are mixed together to form a gel in less than one minute;

b) combining the first and second components in the presence of the drug, under conditions where the first component reacts with the second component.

114. A product produced by the method of claim 113.

115. A method for forming a drug delivery composition, comprising

a) forming an admixture of polyalkylene oxide-$(SH)_4$ and drug in a liquid medium having a pH of between 8 and 10.5; and

b) forming an admixture of polyalkylene oxide-Y_4, wherein Y is succinimidyl and liquid medium, the admixture having an acidic pH.

116. The method of claim 115 further comprising combining the admixtures of steps a) and b).

117. A product produced by the method of claim 116.

118. A method for forming a biocompatible gel-forming drug-delivering composition for *in vivo* administration with a gel time of less than one minute, comprising:

a) preparing an admixture of polyalkylene oxide-$(SH)_{12}$ and drug in a liquid medium having an alkaline pH; and

b) preparing polyalkylene oxide-Y_{12} in a liquid medium having an acidic pH, wherein Y is a succinimidyl or maleimidyl group.

119. The method of claim 118 further comprising combining a) and b).

120. The product produced by the method of claim 119.

121. A method for forming a biocompatible gel-forming composition for *in vivo* administration, comprising:

a) preparing a sulfhydryl group-containing polyalkylene oxide in a liquid medium having an acidic pH, wherein said sulfhydryl group-containing polyalkylene oxide is given by the formula Core-$(SH)_m$, wherein $m \geq 2$;

b) providing a buffer solution with an alkaline pH; and

c) adding drug to either or both of a) and b);

wherein the sulfhydryl groups react with one another to form covalent bonds therebetween when said components are mixed together to form a gel in less than one minute.

122. The method of claim 121 further comprising combining a) and b).

123. The product produced by the method of claim 122.

124. A method for forming a biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

a) providing an at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula $Compound_1$ -$(SH)_m$, wherein $m \geq 2$;

b) providing an at least one sulfhydryl reactive group-containing compound either in a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula $Compound_2$ -Y_n, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$;

c) combining a drug with either or both of the at least one sulfhydryl group-containing compound and the at least one sulfhydryl reactive group-containing compound; and

d) providing collagen;

wherein at least one of either the sulfhydryl group-containing compound or the sulfhydryl reactive group-containing compound is a polyalkylene oxide; and

wherein the sulfhydryl groups and the sulfhydryl reactive groups are capable of reacting with one another to form covalent bonds therebetween.

125. A method for forming a biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

a) providing an at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula $Compound_1$ $-(SH)_m$, wherein $m \geq 2$;

b) providing an at least one sulfhydryl reactive group-containing compound either in a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula $Compound_2$ $-Y_n$, wherein Y is a sulfhydryl reactive group and wherein $n \geq 2$; and

c) providing collagen;

wherein at least one of either the sulfhydryl group-containing compound or the sulfhydryl reactive group-containing compound is a polyalkylene oxide; and

wherein the sulfhydryl groups and the sulfhydryl reactive groups are capable of reacting with one another to form covalent bonds therebetween.

126. The product produced by the method of claim 125.